REMARKS

Claims under Examination

Applicants acknowledge that claims 6-8 are pending.

Summary of the Bases for Rejection

Rejections under 35 U.S.C. § 101 and 102 have been withdrawn. Claims 6-8 stand rejected under 35 U.S.C. § 112, first paragraph (enablement). The Applicants address this basis for rejection below.

Rejection Under 35 U.S.C. § 112, First Paragraph (Enablement)

Applicants thank the Examiner for her insightful and helpful comments given during the telephone interview of January 8, 2008.

Applicants submit that claims 6-8 are enabled under 35 U.S.C. § 112, first paragraph. The instant specification enables one of skill in the art to obtain mesenchymal stem cells (*see, for example*, Specification, pages 6-7 and 13), expand the mesenchymal stem cells in culture (*see, for example*, Specification, page 7), administer the mesenchymal stem cells to a fetus *in utero* (*see, for example*, Specification, pages 14-17), and achieve engraftment in multiple tissue types (*see, for example*, Specification, pages 21-24).

For example, mesenchymal stem cells may be recovered from bone marrow, embryonic yolk sac, placenta, umbilical cord, fetal or adolescent skin, and blood. Specification, page 6, lines 27-32. Mesenchymal stem cells may be isolated, for example, by procedures known in the art and further described in the instant specification. *See, for example*, Specification, page 13,

lines 14-32. Mesenchymal stem cells may be administered to a fetus *in utero* by, for example, intraperitoneal or intravenous injection. Specification, page 14, lines 30-32 and page 16, line 33 to page 17, line 3. Two weeks following administration of human mesenchymal stem cells *in utero*, human cells were present in sheep fetal liver, spleen, bone marrow, thymus, and lung. Specification, page 20, lines 18-20, page 21, lines 13-19, and Figure 6. Five months after administration, human cells continued to be present in multiple tissues including bone marrow, thymus, spleen, lung, cartilage, heart, skeletal muscle, and brain. Specification, page 20, line 24 to page 21, line 3 and page 21, lines 19-21. Moreover, site-specific differentiation of mesenchymal stem cells was confirmed for cardiomyocytes (Specification, page 22, lines 9-17; Figure 7), chondrocytes (Specification, page 22, line 19 to page 23, line 2; Figure 8), bone marrow stromal cells (Specification, page 23, lines 4-14; Figure 9), thymic stromal cells (Specification, page 23, lines 16-25; Figure 10), and brain cells (Specification, page 24, lines 1-8; Figure 11).

Moreover, how a teaching is set forth, by specific example or broad terminology, is not important. *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 370 (CCPA 1971); MPEP § 2164.08. The instant specification broadly states that the present invention relates to the use of human mesenchymal stem cells for *in utero* administration. Specification, page 6, lines 23-25. Moreover, in one embodiment, human mesenchymal stem cells may be administered to a non-human fetus *in utero*. Specification, page 12, lines 17-18. Even if the claimed methods did not work in some species, and the Examiner has not shown that they would not, the Federal Circuit has held:

> It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention.

Capon v. Eshar, 418 F.3d 1349, 1359, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005). Thus, the instant specification enables one of skill in the art to engraft mesenchymal stem cells by administering cells consisting essentially of mesenchymal stem cells to a fetus *in utero* by, for example, broad terminology as well as the specific examples of *in utero* transplantation of xenogeneic mesenchymal stem cells as set forth in the instant specification.

Applicants wish to emphasize that instant claims 6-8 are directed to a method of engrafting mesenchymal stem cells. In that regard, various passages from Bianco cited in the Office Action of July 13, 2007 are concerned with replenishment or regeneration of entire organs or systems. *See* July 13, 2007 Office Action, page 7. Claims 6-8 are not directed to the generation of an entire organ or system but rather, as noted above, to engraftment of mesenchymal stem cells as described and enabled by, for example, Examples 1 and 2 of the instant specification.

The Examiner has previously noted that Applicants have demonstrated a utility for the claimed invention. *See* July 13, 2007 Office Action, page 3, first paragraph. Applicants have noted in previous responses, as well as in the instant specification, that the methods recited by the instant claims may have additional utility in the context of (i) large scale tissue engineering; (ii) cellular therapy for diseases of mesenchymal origin; (iii) bone marrow conditioning; (iv) gene therapy; and (v) immunologic tolerance. However, the instant claims are neither directed to nor limited by any such therapeutic effects or clinical applications. In that regard, to the extent that the post-filing art of Bianco and Flake are focused on therapeutic effects and clinical

applications, the comments and insights contained therein have little applicability to the instant claims.

Finally, Applicants respectfully disagree with the Examiner's assertion that the art indicates that one xenogeneic transplant example is not indicative that other xenogeneic transplants are enabled. The Examiner cites Flake to support this allegation. *See* July 13, 2007 Office Action, page 8. However, Applicants submit that cited passages of Flake support the conclusion that the instant specification enables the full scope of the claims. Flake notes that, as compared to sheep models, a smaller number of donor cells were detected in other species. Flake, page 945, paragraphs 1-2. Flake, however, does not teach or suggest that some level of engraftment was not achieved in other species, but rather only that the number of engrafted cells may be lower in some species as compared to sheep. Indeed, high rates of durable engraftment are achievable in species other than sheep; albeit with a lower degree of engraftment. Thus, the cited passages of Flake contradict the Examiner's assertion that one xenogeneic transplant example is not indicative that other xenogeneic transplants are enabled.

Therefore, for at least the reasons discussed above, the Applicants respectfully submit that a method of engrafting mesenchymal stem cells by administering cells consisting essentially of mesenchymal stem cells to a fetus *in utero* is enabled by the instant specification, and the rejection of claims 6-8 under the enablement requirement of 35 U.S.C. § 112, first paragraph should be withdrawn.

CONCLUSION

If the Examiner has additional questions or the Applicants can be of further assistance, the Examiner is invited and encouraged to contact the Applicants' attorney at the number below.

The Commissioner is authorized to charge any necessary fees or credit any overpayment to the Deposit Account of McAndrews, Held & Malloy, Ltd., Account No. 13-0017.

Respectfully submitted,

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